Remarks

Reconsideration of this Application is respectfully requested. Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Status of the Claims

Upon entry of the foregoing amendment, claims 48 and 76-80 are pending in the application, with all of the pending claims being independent claims. Claims 49-75 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Claim 48 is hereby amended. New claims 76-80 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

II. The Amendment

Claim 48 has been amended to more particularly point out what Applicants regard as the invention. Specifically, the claim has been amended to recite "a method of treating pain resulting from C-fiber neuron activity . . .," as suggested by the Examiner during a telephonic conversation on October 19, 2006. In addition, support for this amendment can be found, *inter alia*, at page 1, lines 3-7 and 9-10, and page 4, lines 15-17. Further, the term "first" has been deleted from the claim, and the claim now recites the lectin as an *Erythrina cristagalli* lectin (ECL). Basis for this amendment can be found, *inter alia*, at page 6, lines 30-32. Support for new claims 76 and 77 can be found, *inter alia*, in Example 8 and Figure 5, and Example 7 and Figure 4, respectively. Support for new claim 78 can be found, *inter alia*, in Examples 14 and 18, and in Figures

10 and 13. Support for new claim 79 can be found, *inter alia*, in Example 8 and Figure 5, and page 8, lines 14-21. Support for new claim 80 can be found, *inter alia*, in Example 7 and Figure 4, and page 8, lines 14-21. Accordingly, entry of this amendment is respectfully requested.

III. Objection to the Claim

At page 4 of the Office action, the Examiner has objected to claims 48-53 on the ground that the recitation of "first" lectin in claims 48 and 52 renders the claims confusing, "since there is no 'second' lectin ever claimed." Solely for the purpose of expediting prosecution without acquiescing to the Examiner's rejection, the term "first" has been deleted from claim 48. Claims 49-53 have been cancelled, thus rendering the objection moot. Applicants respectfully request reconsideration and withdrawal of this objection.

IV. The Rejection Under 35 U.S.C. § 112, First Paragraph Written-Description

At pages 5-6 of the Office action, the Examiner has rejected claims 48-53 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention, at the time of filing of the application. More specifically, the Examiner alleges that "the specification has adequately described the use of a single ECL conjugate (e.g. the conjugation of ECL to the clostridial enzyme designated LH_N/A (See Example 3)), in a method of treating two (2) C-fibre associated diseases or conditions: pain . . . and . . . inflammation. However,

there is no description as to how or whether any lectin/ECL alone (or any other conjugate for that matter) would be able to inhibit or stimulate any C-fibre neuron activity/diseases or conditions thereto." Applicants respectfully traverse the rejection

Applicants assert that the specification expressly teaches ECL and at least two other specific lectins, *Bandeiraea simplicifolia* lectin (IB_4) and *Triticum vulgaris* wheat germ agglutinin lectin (WGA), for inhibiting C-fibre neuron activity, and thereby treating pain (e.g. creating analgesic effect in mice) and inflammation. In addition, prior to the present invention, a person having ordinary skill in the art would have been familiar with the link between stimulation of C-fibres and pain and/or inflammation.

First, Example 14 and Figure 10 clearly teach that galactosyl-binding lectin ECL inhibits C-fibre neuron activity *in vitro* by preventing the release of a key neurotransmitter - substance P. *See* page 31-32 and Figure 10. Further, Example 16 and Figure 12 confirm that administration of ECL also inhibits C-fibre neuron activity *in vivo*. *See* page 33 and Figure 12. As indicated in Figure 12, a downward trend in C-fibre neuron activity is observed following administration of ECL. Further, Example 5 and Figure 2 show that ECL-induced analgesia is similar to that of a 10 μg/mouse supramaximal (20 times the mouse EC50) of morphine but is of much longer duration; morphine achieves a maximal effect at 1 hour and then declines over a period of 5 hours. Page 23, lines 21-26. In contrast, lectin-induced analgesia reaches a maximum within 1 hour of administration and remains constant for at least 5 hours. *Id.* Such long-lasting effect is achieved through the inhibition of neurotransmitter/neuromodulator release from C-fibres and consequent inhibition of C-fibre neuron activity, as discussed above. Finally, Example 19 and Figure 14 confirm that increasing dosages of ECL provide an

analgesic effect, as demonstrated by increased paw-withdrawal time in the mouse hot-plate test. *See* pages 37-39.

Similarly, Example 7 and Figure 4 disclose the use of glucosyl-reactive WGA from *Triticum vulgaris* in inhibiting C-fibre neuron activity *in vivo*. *See* page 25 and Figure 4. Example 8 and Figure 5 disclose the use of galactosyl-reactive lectin IB_4 from *Bandeiraea simplicifolia* in achieving an analgesic effect *in vivo*. *See* pages 25-26 and Figure 5. The analgesic effect generated by WGA and IB_4, consistent with ECL, is achieved through the inhibition of neurotransmitter/neuromodulator release from C-fibres.

Second, Example 18 and Figure 13 explicitly disclose that administration of ECL reduces extravasation induced by antidromic C-fibre activity, thereby decreases neurogenic inflammation. Page 35, lines 5 to page 37, lines 1-15, and Figure 13. *See* also page 1, lines 21-32.

Accordingly, based on the full disclosure of the use of three specific lectins alone in treating pain and/or inflammation in the specification, one of ordinary skilled in the art would recognize that Applicants were in possession of the claimed method of inhibiting C-fibre neuron activity/associated diseases or conditions in using a lectin alone, including ECL, IB_4, and WGA, at the time of filing.

Thus, there is no basis on which to reject claim 48 under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement, and the Examiner's rejection is improper. In addition, claims 49-53 have been cancelled, thus rendering moot the rejection of these claims. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. The Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

At pages 7-9 of the Office action, claims 48-53 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for treatment of any C-fibre neuron associated diseases/conditions by any lectin alone or the elected species ECL.

The Examiner first alleges that the nature of the invention, according to the *In re Wands* factors, is drawn to the use of any lectin or species ECL alone to inhibit or stimulate C-fibre neuron activity to treat any disease or condition resulting from inhibition or stimulation of C-fibre neuron activity. Applicants respectfully traverse the rejection.

As discussed above at pages 5-7, the nature of the claimed invention relates to the use of specific lectins for inhibiting C-fibre neuron activity to treat disease or condition resulting from C-fibre neuron activity. Further, as presently amended, claim 48 is directed to a method of treating pain resulting from C-fibre neuron activity using ECL. Thus, the claimed invention is drawn to a specific lectin for a specific use.

The Examiner then asserts that there are no working examples in the specification to indicate whether any lectin/ECL alone would be enabled for treating any C-fibre neuron disease/condition. Applicants again respectfully traverse the rejection.

As discussed in detail at pages 5-7, *supra*, specific examples and figures in the specification explicitly disclose the use of specific lectins, including ECL, IB_4, and WGA, as a method of treating pain and inflammation resulting from C-fibre neuron activity.

Finally, the Examiner states that under the factors of the breadth of the claims and the quantity of experimentation needed, in the absence of sufficient teachings in the specification, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims,. Applicants disagree.

The specification not only provides specific teachings of the use of three specific lectins in treating pain or inflammation, as discussed at pages 5-7, but also requires no undue experimentation by one of skill in the art to practice the invention. For example, the specification teaches the use of mouse hot plate model for testing the analgesic effects of ECL, IB4, and WGA. *See* Examples 7, 8, and 19. Such test is an industry standard model acknowledged as predictive of human response. Page 6, lines 18-24.

In addition, the cancellation of claims 49-53 render the rejection of these claims moot.

In view of the above, the Examiner's rejection of claims 48-53 under 35 U.S.C. § 112, first paragraph, is improper. Reconsideration and withdrawal of the rejection is respectfully requested.

VI. The Rejection Under 35 U.S.C. § 112, Second Paragraph-Indefiniteness

At pages 9-10, claims 48-53 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite and failing to point out and claim the subject matter which Applicants regard as the invention. More specifically, the Examiner states that:

> [a]pplicant's elected invention is a method of treating a disease or condition resulting from an inhibition or stimulation of C-fibre neuron activity, by modulating C-fibre activity, comprising administering an effective

> amount of an Erythrina cristagalli lectin *conjugate* (*claim 1*); wherein said *conjugate* may inhibit (*claim 40*) or stimulate (*claim 41*) C-fibre activity. It is unclear how an Erythrina cristagalli lectin can both inhibit and stimulate C-fibre activity, in order to treat a disease or condition resulting from an inhibition or stimulation of C-fibre neuron activity?

Id (emphasis added). Applicants respectfully traverse the rejection.

To begin with, claims 1, and 40-41 reciting ECL conjugate are *not* within the scope of claims 48-53. Assuming *arguendo* that the Examiner intends the term ECL conjugate to be ECL, solely for the purpose of expediting prosecution without acquiescencing to the Examiner's rejection, Applicants have amended claim 48 to recite that ECL is used to only inhibit C-fibre neuron activity as a method of treating pain resulting from C-fibre neuron activity. Furthermore, the new claims 76-80 do not recite any method of "stimulating," only "inhibiting" C-fibre neuron activity.

Cancellation of claims 49-53 renders the rejection of these claims moot.

Accordingly, Applicants respectfully submit that for the reasons stated above, the Examiner's rejection of claims 48-53 under 35 U.S.C. § 112, second paragraph, is improper and request its withdrawal.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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